Diagnosis of acute rheumatic carditis: An echo in time…

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One of the many enduring debates in the management of patients with acute rheumatic fever (ARF) concerns the role of echocardiography in diagnosing acute carditis. Uncertainty regarding its utility persists because there is little reliable prospective follow-up of acute carditis in the echocardiographic era. The ideal study design to address this question (a diagnostic randomized trial with progression to chronic valvular heart disease as the primary outcome) is difficult to implement and is unlikely to ever be performed. A prospectively assembled cohort of a reasonable number of patients with long-term follow-up presents the next best option. However, the available prospective study data is of poor quality and involves <100 patients in all, most followed up for only about 2 years.[1] Therefore, we need to draw inferences from retrospective studies, while keeping in mind the limitations of such a design.

In this issue of the Journal, Araújo and colleagues.[2] present the results of a retrospective analysis of patients with ARF who had echocardiography in the acute phase. These investigators have reported their analyses previously, but the current report presumably presents the most updated results with the largest number of patients with both clinical and echocardiographic data.

AGREEMENT BETWEEN CLINICAL CARDITIS AND ECHOCARDIOGRAPHIC VALVULITIS

The prevalence of subclinical carditis observed in this study was about 16% (72/462) which is consistent with the estimate from a previous systematic review and meta-analysis.[1] The authors report a *kappa* value of 0.48 which represents poor agreement (not good agreement as the authors suggest) between clinical and echocardiographic carditis. However, a better estimate of agreement can be obtained using the weighted *kappa* in situations where concordance between multiple ordinal variables is assessed. To illustrate, in this study the authors evaluated if a diagnosis of clinical carditis (characterized as absent, mild, moderate or severe) was concordant with that diagnosed by echocardiography. It is intuitive that characterization by one modality as mild carditis and the other as moderate carditis constitutes less disagreement than characterization by one as no carditis and the other as severe carditis. Weighting takes into account the degree of disagreement. The weighted *kappa* estimated from the authors' dataset is 0.66, which may be considered good agreement. However, it is important to carefully consider the nature of the observed disagreement between clinical and echocardiographic carditis in order to understand its implications. Table 1 in their study suggests that 60 of the 72 patients missed by clinical examination had mild carditis and 12 had moderate carditis. Approximately half the patients with mild clinical carditis (65/135) turned out to have moderate carditis on echocardiography. As we shall see below, this has implications for prognosis.

PREDICTORS OF CHRONIC VALVULAR HEART DISEASE

In keeping with previous observations, the authors show that the presence and severity of carditis in the initial episode, and the frequency of recurrent ARF, are all associated with the development and progression of chronic valve disease. Although the authors have not presented any data regarding this, the recurrences were presumably related to irregular prophylaxis. However, the conclusion by the authors, that the presence of arthritis or chorea in the acute episode is protective for valve disease in the future, is an error of interpretation. Because carditis, arthritis and chorea are the major determinants of a diagnosis of ARF in the overwhelming majority of patients, it is in fact the absence or relative paucity of concomitant carditis among patients with arthritis and chorea, which protects against the development of chronic valve disease.

Table 1: Probability* of progression to chronic valve disease for patients with ARF with or without carditis

Severity of carditis	Clinical assessment	Echocardiography
No carditis	0.25	0.04
Mild carditis	0.93	0.76
Moderate carditis	0.95	0.97
Severe carditis	1.00	1.00

*Probabilities are for developing any severity of chronic valvular heart disease

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PROGRESSION TO CHRONIC VALVULAR HEART DISEASE AND THE CRITICAL ROLE OF ECHOCARDIOGRAPHY

In this study, patients were enrolled when they had ARF and were then followed up for an average of 9.4 years. Chronic valve disease was diagnosed by experienced clinicians and there was apparently no loss to follow-up. Therefore, although the data was retrospectively collected, it allows us to calculate the likelihood of chronic valve disease occurring among patients with carditis during the index episode of ARF. Table 1 presents the probability of occurrence of chronic valve disease during follow-up for varying degrees of clinical and echocardiographic carditis. Three important inferences can be drawn from this data: (1) A quarter of the patients declared as not having carditis on clinical examination alone will develop chronic valvular heart disease on follow-up, (2) About a quarter of the patients with mild echocardiographic carditis will not have chronic valve disease on follow-up, and (3) The vast majority of patients with moderate, and all patients with severe carditis will go on to develop chronic valve disease, irrespective of whether they were diagnosed clinically or by echocardiography. The apparently high likelihood of progression of clinically detected mild carditis is probably because of misclassification of some patients with moderate valvulitis as mild on clinical examination.

These data in turn allow us to estimate the incremental benefit of echocardiography over clinical examination alone during the acute phase of carditis. From Table 1 in the study by Araújo, and the probabilities depicted in the table above, we can determine that, of the 72 patients missed by clinical examination, approximately 58 ($12 \times 0.97 = 12$, and $60 \times 0.76 = 46$) will go on to develop chronic valve disease. This translates to about 124 patients with chronic valve disease for every 1000 patients evaluated without echocardiography during the acute episode of RF. Of these, 109 patients will develop mild valve lesions, 14 moderate lesions and 2 severe lesions (calculations based on data from table 2 in the paper[2]). However, it is important to bear in mind that these are merely estimates which are likely to vary over a range of values around these estimates.

In summary, the present study lends support to previous data demonstrating superior diagnostic performance of echocardiography compared to clinical criteria alone in the diagnosis of acute rheumatic carditis,[2-5] and provides some quantitation of this benefit in terms of progression to chronic valve disease. Although echocardiography in ARF may or may not lead to treatments which directly result in reduction of progression to chronic valve disease, it may encourage patient compliance to secondary prophylaxis and prescription of more intensive regimens (2 or 3-weekly vs. 4-weekly) continued for a longer period of time. At least some of these measures may reduce progression to chronic valve disease.[4-6] Access to echocardiography is improving even in low-resource settings because of technological advancements contributing to miniaturization and improved portability, and reduced costs. Therefore, in all patients with suspected ARF, every attempt must be made to perform an echocardiogram within the first 12 weeks of the episode. In resource-poor settings, it is often not possible to perform an echocardiogram at the time of clinical examination, and this flexibility in timing will improve feasibility in most situations. If carditis is diagnosed using currently accepted echocardiographic criteria, patients should qualify for secondary prophylaxis irrespective of the results of clinical evaluation.[7] An echocardiogram performed in time may prevent carditis from going unrecognized, and perhaps untreated.

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